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## -continued

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val 200 Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr 220 Lys Ser Phe Asn Arg Gly Glu Cys (2) INFORMATION FOR SEQ ID NO:26: (i) SEQUENCE CHARACTERISTICS: (A) LENGTH: 122 amino acids (B) TYPE: Amino Acid (D) TOPOLOGY: Linear (xi) SEQUENCE DESCRIPTION: SEQ ID NO:26: Glu Val Gln Leu Val Glu Ser Gly Gly Gly Leu Val Gln Pro Gly 1 5 10 15 Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Tyr Ser Phe Thr  $20 \\ 25 \\ 30$ Gly Tyr Thr Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu  $35 \hspace{1cm} 40 \hspace{1cm} 45$ Glu Trp Val Ala Leu Ile Asn Pro Tyr Lys Gly Val Thr Thr Tyr  $50 \\ 55 \\ 60$ Ala Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Val Asp Lys Ser  $65 \\ 70 \\ 75$ Lys Asn Thr Ala Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp  $80 \\ 80 \\ 85$ Thr Ala Val Tyr Tyr Cys Ala Arg Ser Gly Tyr Tyr Gly Asp Ser  $95 \\ 1 \\ 00 \\ 1 \\ 05$ 

Ser Ser 122

We claim:

1. A humanized antibody variable domain comprising non-human Complementarity Determining Region (CDR) amino acid residues which bind an antigen incorporated into a human antibody variable domain, and further comprising a Framework Region (FR) amino acid substitution at a site selected from the group consisting of: 4L, 38L, 43L, 44L, 58L, 62L, 65L, 66L, 67L, 68L, 69L, 73L, 85L, 98L, 2H, 4H, 36H, 39H, 43H, 45H, 69H, 70H, 74H, and 92H, utilizing the numbering system set forth in Kabat.

Asp Trp Tyr Phe Asp Val Trp Gly Gln Gly Thr Leu Val Thr Val

- 2. The humanized variable domain of claim 1 wherein the substituted residue is the residue found at the corresponding location of the non-human antibody from which the non-human CDR amino acid residues are obtained.
- 3. The humanized variable domain of claim 1 wherein no human Framework Region (FR) residue other than those set forth in the group has been substituted.
- **4.** The humanized variable domain of claim **1** wherein the human antibody variable domain is a consensus human 60 variable domain.
- 5. The humanized variable domain of claim 1 wherein the residue at site 4L has been substituted.
- 6. The humanized variable domain of claim 1 wherein the residue at site 38L has been substituted.
- 7. The humanized variable domain of claim 1 wherein the residue at site 43L has been substituted.

- 8. The humanized variable domain of claim 1 wherein the residue at site 44L has been substituted.
- 9. The humanized variable domain of claim 1 wherein the residue at site 58L has been substituted.
- 10. The humanized variable domain of claim 1 wherein the residue at site 62L has been substituted.
- 11. The humanized variable domain of claim 1 wherein the residue at site 65L has been substituted.
- 12. The humanized variable domain of claim 1 wherein the residue at site 66L has been substituted.
- 13. The humanized variable domain of claim 1 wherein the residue at site 67L has been substituted.
- 14. The humanized variable domain of claim 1 wherein the residue at site 68L has been substituted.
- 15. The humanized variable domain of claim 1 wherein the residue at site 69L has been substituted.
- 16. The humanized variable domain of claim 1 wherein the residue at site 73L has been substituted.
- 17. The humanized variable domain of claim 1 wherein the residue at site 85L has been substituted.
- 18. The humanized variable domain of claim 1 wherein the residue at site 98L has been substituted.
- 19. The humanized variable domain of claim 1 wherein the residue at site 2H has been substituted.
- 20. The humanized variable domain of claim 1 wherein the residue at site 4H has been substituted.